



Personality Disorders And Clinical Response To Intranasal Esketamine In Treatment-resistant Depression: Trajectories, Modulations And Psychopathological Reflections

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INTRODUCTION

Intranasal Esketamine is an established treatment for Treatment-Resistant Depression (TRD), although response trajectories show substantial interindividual variability.

Personality Disorders (PDs), highly prevalent in TRD, may influence both the magnitude and temporal pattern of antidepressant response. However, their specific impact on Esketamine outcomes remains insufficiently characterized.

STUDY AIM

To examine differential response trajectories to intranasal Esketamine across distinct personality disorder structures.

METHODS

Prospective naturalistic observational study including 60 adults with TRD (failure of ≥ 2 antidepressant treatments) recruited from outpatient TRD clinics in Milan and Pavia.

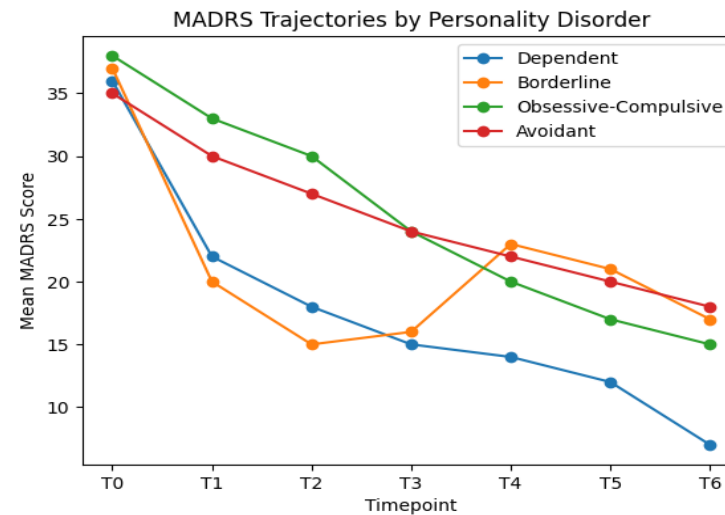
PD diagnoses were established using SCID-5-PD and patients were stratified into four groups (n = 15 each): Borderline, Obsessive-Compulsive, Dependent, and Avoidant PD.

Esketamine was administered intranasally (56–84 mg) twice weekly for 4 weeks, then weekly.

Depressive symptoms were assessed weekly using MADRS from baseline (T0) to week 6.

Mixed-model analysis evaluated time \times group interaction effects.

RESULTS



All groups showed significant MADRS reduction over time. However, a significant time \times group interaction emerged ($p < 0.001$), indicating distinct response trajectories.

- **Dependent PD:** rapid symptom reduction from week 1.
- **Borderline PD:** early improvement (weeks 1–2) followed by partial symptom rebound at weeks 4–5.
- **Obsessive-Compulsive PD:** delayed but progressive and stable response (\geq week 3).
- **Avoidant PD:** moderate, steady improvement across timepoints.

Between-group effect size at week 4 was large (Cohen's $d = 1.52$).

CONCLUSIONS

Personality disorder structure significantly modulates the temporal pattern of clinical response to intranasal Esketamine in Treatment Resistant Depression (TRD).

While overall antidepressant efficacy was observed across groups, trajectory differences suggest that personality-related affective and interpersonal styles may influence response stability and timing.

Routine assessment of personality pathology in TRD patients receiving Esketamine may improve prediction of response trajectories and inform personalized monitoring strategies.

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